DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
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January 3, 2015

Coramed Technologies, LLC
c/o Mr. Norman Brunner
Director of RA/QA
6225 W. Howard Street
Niles IL 60714

Re: k140893
Trade/Device Name: CORA (Coagulation Resonance Analysis) System with Platelet Mapping Assay
Regulation Number: 21 CFR 864.5700
Regulation Name: Automated platelet aggregation system
Regulatory Class: II
Product Code: JOZ
Dated: December 2, 2014
Received: December 3, 2014

Dear Mr. Brunner:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the

electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Leonthena R. Carrington -A

for Mary S. Pastel, ScD
Deputy Director for Radiological Health
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K140893

Device Name
CORA PlateletMapping Hemostasis System

Indications for Use *(Describe)*
The CORA PlateletMapping System consists of the CORA analyzer and the CORA PlateletMapping Assay Cartridge. The CORA Platelet Mapping System is intended for in vitro diagnostic use to provide qualitative assessment of platelet function. The CORA System records the kinetic changes in a sample of heparinized whole blood as the sample clots.

The CORA System PlateletMapping Assay Cartridge provides four channels of dried-in-place reagents, HKH (Kaolin with Heparinase), Activator F, AA and ADP (one reagent in each channel). In combination, MA parameter results from these four reagents are used to calculate the parameters platelet % Inhibition and % Aggregation for AA and ADP.

Results from the CORA analysis should not be the sole basis for a patient diagnosis, but should be evaluated together with the patient's medical history, the clinical picture and, if necessary, further hemostasis tests.

The CORA System with CORA PlateletMapping Assay Cartridge is indicated for use with adult patients where an evaluation of their blood hemostasis properties is desired. Hemostasis evaluation with the CORA PlateletMapping System is used to assess clinical conditions in cardiovascular surgery and cardiology procedures to assess hemorrhage or thrombosis conditions.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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Coramed Technologies, LLC
6225 W. Howard Street, Niles, Illinois 60714
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CORA® System PlateletMapping Assay 510(k) Summary

APPLICANT INFORMATION

Name of Manufacturer: Coramed Technologies, LLC

Manufacturer Street Address: 6225 W. Howard St.

City, State, Zip: Niles, IL 60714

Phone Number: (847) 647-8800

FAX Number: (847) 510-0502

Contact person for all communications: Norman E. Brunner

Email for contact person: nbrunner@coramedtech.com

Date that Summary was prepared: January 2, 2015

DEVICE INFORMATION

Trade name (proprietary name): CORA® (Coagulation Resonance Analysis) System and the following assays and reagents

- PlateletMapping® Assay Reagents (heparinized blood)
  - HKH (Kaolin with Heparinase), Kaolin + Heparinase
  - ActF (ActivatorF)
  - ADP (adenosine-5'-diphosphate)
  - AA (Arachidonic Acid)

Common name (usual name): Whole Blood Hemostasis System

Classification Name: 21CFR 864.5700 Automated Platelet Aggregation System

PREDICATE DEVICE

- Thrombelastograph® (TEG® PlateletMapping Assay), K041502, Product Code JOZ (System, Automated Platelet Aggregation), Haemoscope Corporation

DESCRIPTION OF THE DEVICE

System Description

The CORA PlateletMappingSystem consists of a four-channel diagnostic analyzer with integrated computer module, system reagents (ActF, AA, ADP and HKH) and microfluidic test cartridge. See below for a description of system reagents. Reagents are dried-in-place within the cartridges during manufacturing.

To perform a test, a disposable CORA PlateletMapping Assay Cartridge is inserted into the analyzer. Blood is added to an entry port on the cartridge and drawn into the cartridge under analyzer control. The amount of the sample drawn into the cartridge is automatically determined by the volume of the blood chambers in the cartridge. Once in the disposable, the sample is metered into as many as four separate analysis channels, depending upon the assay being performed. Reconstitution of reagents dried within the cartridge is accomplished by moving the sample back and forth through reagent chambers, under the control of microfluidic valves and bellows within the cartridge. After each sample has been mixed with reagent, it is delivered to a test cell where it is monitored for changes due to coagulation. Excess sample material is moved under microfluidic control into an enclosed waste chamber within the cartridge.

The CORA Measurement Technique

The CORA technology is based on a disposable containing up to four independent measurement cells. Each cell consists of a short vertically-oriented injection molded tube (ring) with a diameter of 2.5mm and a length of 4.5mm. Detection of clotting in the CORA System is performed optically. Under control of the analyzer, approximately 20µL of prepared sample is delivered to the tube, where a meniscus naturally forms at each end of the tube. The tube is positioned so that the lower meniscus partially blocks light traveling from a collimated source toward a photodiode.

During testing, a piezoelectric actuator drives the measurement cell(s) through a motion profile composed of summed sinusoids at different frequencies. The profile has a maximum amplitude of under 10µm and contains frequencies from 10-500Hz. Some, but not all, of the measurement cell motion will induce motion in the sample meniscus, which will be detected by the photodiode. The resulting motion of the meniscus is monitored optically and analyzed by the analyzer to calculate the resonant frequency and modulus of elasticity (stiffness) of the sample. By performing a Fast Fourier Transform (FFT) on meniscus motion data, it is possible to determine the frequencies of input motion that caused the greatest deflection of the sample (these are called the resonant frequencies).

Resonance is the tendency of a material or structure to oscillate with greater amplitude at some frequencies than others. The exact frequencies at which resonance occurs will depend on the stiffness and mass of the sample. Stiffness, in turn, is a function of a material's modulus of elasticity and the boundary conditions to which the material is exposed, such as the geometry and materials of a test cell. By holding these boundary conditions and sample mass constant from run to run, the CORA System allows direct comparison of elasticity between samples.

In a typical test, blood that has been delivered to the measurement cell will not clot for several minutes. During this time the sample has no inherent stiffness except that provided by surface tension, and since this remains constant the measured resonant frequencies will not change. Once clotting begins, however, the elastic modulus and thus the resonant frequencies increase rapidly. In tests where clotting does not occur, the resonant frequency of the sample will not change. During coagulation, however, a clot will bind to the test tube (ring) and the resonant frequency will rise with increasing firmness of the clot. The CORA Analyzer collects meniscus motion data, tracks changing resonant frequencies and analyzes the frequency data to provide parameters describing the clot. Results are presented in a format identical to the TEG 5000.

The following definitions apply to calculated parameters in the CORA System:

CORA Parameter	Definition	Purpose
MA	MA, or Maximum Amplitude, represents the maximum firmness of the clot during the test.	Normal / reduced / increased clot elasticity/strength
ADP %Aggregation	See below	Level of ADP platelet activity aggregation
ADP %Inhibition	See below	Level of ADP platelet activity inhibition
AA %Aggregation	See below	Level of AA platelet activity aggregation
AA %Inhibition	See below	Level of AA platelet activity inhibition

PlateletMapping Assay and Reagents

The assay uses AA and ADP agonists to assess platelet aggregation or inhibition. Since thrombin (present in blood samples) is the primary and most potent activator of platelets, its activity must be inhibited with heparin so that the platelet inhibiting effects of ADP and AA can be measured. Thrombin also converts fibrinogen into fibrin to create the fibrin mesh necessary for any clot formation, and converts Factor XIII to Factor XIIIa for fibrin cross linking. Since thrombin has been rendered inactive by heparin, ActivatorF is used to replace thrombin's role in the conversion of fibrinogen to fibrin and Factor XIII to Factor XIIIa. Thus, with this cross-linked fibrin network as the foundation (represented by MA_{ActF}), additional clot strength due to platelet-fibrin bonding related to ADP (MA_{ADP}) and AA (MA_{AA}) platelet receptor activation can be measured. The HKH reagent, a combination of Kaolin and Heparinase, generates test data for the uninhibited MA (MA_K) resulting from thrombin activation of the blood sample, while the Heparinase neutralizes the effects of heparin.

For calculations of clot strength reduction, percent MA reduction is

$$100 - \left[\left\{\frac{MA_P - MA_{ActF}}{MA_K - MA_{ActF}}\right\} * 100\right], \quad \textit{(Equation 1)}$$

where MA_P can be either MA_{ADP} or MA_{AA}. AA Aggregation and Inhibition, and ADP Aggregation and Inhibition are parameters derived from the CORA MA parameters for the ActF, AA, ADP and HKH reagents, as described above. Following are the equations used by the CORA System to derive these parameters:

AA Percent Aggregation = $\left[\left\{\frac{MA_{AA} - MA_{ActF}}{MA_K - MA_{ActF}}\right\} * 100\right]$, (maximum of 100%) (*Equation 2*)

ADP Percent Aggregation = $\left[\left\{\frac{MA_{ADP} - MA_{ActF}}{MA_K - MA_{ActF}}\right\} * 100\right]$, (maximum of 100%) (*Equation 3*)

AA Percent Inhibition = 100 – AA Percent Aggregation, (minimum of 0%) (*Equation 4*)

ADP Percent Inhibition = 100 – ADP Percent Aggregation, (minimum of 0%) (*Equation 5*)

INTENDED USE AND INDICATIONS FOR USE

The CORA PlateletMapping System consists of the CORA analyzer and the CORA PlateletMapping Assay Cartridge. The CORA Platelet Mapping System is intended for *in vitro* diagnostic use to provide qualitative assessment of platelet function. The CORA System records the kinetic changes in a sample of heparinized whole blood as the sample clots.

The CORA System PlateletMapping Assay Cartridge provides four channels of dried-in-place reagents, HKH (Kaolin with Heparinase), Activator F, AA and ADP (one reagent in each channel). In combination, MA parameter results from these four reagents are used to calculate the parameters platelet % Inhibition and % Aggregation for AA and ADP.

Results from the CORA analysis should not be the sole basis for a patient diagnosis, but should be evaluated together with the patient's medical history, the clinical picture and, if necessary, further hemostasis tests.

The CORA System with CORA PlateletMapping Assay Cartridge is indicated for use with adult patients where an evaluation of their blood hemostasis properties is desired. Hemostasis evaluation with the CORA PlateletMapping System is used to assess clinical conditions in cardiovascular surgery and cardiology procedures to assess hemorrhage or thrombosis conditions.

SUMMARY OF TECHNOLOGICAL CHARACTERISTICS COMPARING THE CORA SYSTEM TO THE TEG 5000 PREDICATE DEVICE

Table of Similarities

Item	TEG® 5000 Platelet Mapping Predicate	CORA® System Platelet Mapping
Analyzer		
Technological Purpose	Monitoring the response of a clot to low levels of applied strain	Monitoring the response of a clot to low levels of applied strain
What is measured	Changes in clot elasticity over time	Changes in clot elasticity over time
Initial Warm Up Time	5 min	5 min
Time to Complete a Test	Varies with assay	Same as TEG 5000
Assays and Reagents		
Platelet Mapping Assay	ActF, AA, ADP and Kaolin with Heparinase	ActF, AA, ADP and HKH reagents, same materials as TEG 5000

Table of Differences

Item	TEG® 5000 Predicate	CORA® System
Analyzer	Thrombelastography analyzer, separate computer and software	Fully integrated Thrombelastography analyzer
Measuring Technique	Direct-contact measurement of shear elasticity of a coagulating sample	Non-contact measurement of shear elasticity of a coagulating sample
Measuring Channels	2, each independent and interchangeable	4, each independent and interchangeable
Signal Transducer	Electromechanical detection (rotary variable inductive transformer) of rotary motion of a pin suspended in the sample	Optical detection (silicon photodiode) of the motion of a free surface of the sample
Temperature Control	20° to 40°C	20° to 50°C
Sample Volume (per channel)	360-380 µL	63µL
Total Reaction Volume (single channel)	360-380µL	20µL
Mains Supply Voltage	120V, 60Hz and 220V, 50Hz model available	100-240V, 50-60Hz (international power supply)
Analyzer Input Voltage	24 volts AC, 30 watts max	12 volts DC, 60 watts max
Environment	Level and vibration free position, no solar radiation Operating temperature: 10° to 35°C Storage Temperature: -30° to 50°C (analyzer only) Relative humidity 20 to 80% (non-condensing)	Stable and level surface Operating Temperature 10° to 32°C Storage Temperature: -20° to 50°C (analyzer only) Relative humidity 20 to 80% (non-condensing)
Sample Preparation	Performed by the operator using pipettes to reconstitute reagents and mix reagents with the sample	Performed under analyzer control within the disposable cartridge
Pipetting	Manual accurate pipettes (10, 20, 50, 100, 340, 360, 500, 1000µL)	Unmetered transfer pipette or syringe; blood sample is added until it fills to a level above the line marked on the blood intake well of the cartridge
Consumables	Cups & Pins (acrylic plastic)	Carrier (acrylic plastic) with microfluidics laminate and test rings (acrylic plastic)

SUMMARY OF NON-CLINICAL PERFORMANCE DATA

Analytical Precision

Testing was performed in Coramed's laboratory for precision, using CLSI EP5-A2 as guidance.

Three types of donor heparinized whole blood (CWB) samples were used in precision testing for the HKH reagent:

- Hypo (donors with naturally low coagulation levels, as indicated by MA parameter near the lower limit of the reference range);
- Normal (donors with natural coagulation levels of MA parameters near the center of the reference ranges):
- Hyper (donors with naturally high coagulation levels, as indicated by and MA parameter near the upper limit of the reference range.

For ADP and AA Aggregation and Inhibition Precision testing, sample types to be used are:

- Normal (donors with little or no platelet inhibition, inhibition levels well below cut-off values)
- Abnormal (donors with platelet inhibition levels above cut-off values)

Testing was performed with blood draws from three donors (one Hypo, one Normal, and one Hyper) for HKH and two donors (Normal and Abnormal) for AA and ADP Percent Aggregation and Inhibition, on each of five days (non-consecutive). Testing was performed by two operators using three reagent lots and twelve analyzers, two replicates. The structure of this precision test is shown below.

Sample Type (Hypo, Normal or Hyper)												
	Day 1 (Total of 5 days)											
Operator	Operator 1						Operator 2					
Reagent lot	1		2		3		1		2		3	
Analyzer	1	2	3	4	5	6	7	8	9	10	11	12
Replicates	1,2	1,2	1,2	1,2	1,2	1,2	1,2	1,2	1,2	1,2	1,2	1,2

Structure of Precision Testing

Precision test estimates by test, parameter and donor sample test level are shown in the table on the following page.

Test	Parameter	Level	n	Mean	Reagent Lot		Operator[1]		Analyzer (within Operator, Reagent Lot)		Day (within Analyzer, Operator, Reagent Lot)		Repeatability		Total[2]	
					SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
HKH	MA	Hypo	120	59.6	0.35	0.6%	0.22	0.4%	0.00	0.0%	0.96	1.6%	0.39	0.6%	1.12	1.9%
HKH	MA	Hyper	120	67.6	0.11	0.2%	0.07	0.1%	0.00	0.0%	0.56	0.8%	0.46	0.7%	0.74	1.1%
HKH	MA	Normal	120	63.4	0.30	0.5%	0.28	0.4%	0.00	0.0%	0.34	0.5%	0.57	0.9%	0.78	1.2%

[1]Operator includes operator and operator-by-reagent lot interaction

[2]Total includes reagent lot, operator, operator-by-reagent lot interaction, analyzer (within operator, reagent lot), day (within analyzer, operator, reagent lot) and repeatability

The percent positive and negative agreement for the AA and ADP % aggregation/inhibition at low and high level platelet function samples was 100%.

Interference

Testing was performed in Coramed's laboratory for interference, using CLSI EP7-A2 as guidance.

For PlateletMapping Assays ActF, AA and ADP, potential interferents tested were Short Draw and Hemodilution. AA and ADP were also tested for interference with Hemolysis. For ActF, no interferents were found. For AA, Hemolysis and Short Draw (less than 2.5 mL in a 4 mL tube) were found to be interferents. For ADP, Short Draw (less than 2.5 mL in a 4 mL tube) and Hemodilution levels above 40% were found to be interferents. HKH potential interferents tested were Absence of a Discard Tube, Short Draw, Hemolysis, Hemodilution and epsilon aminocaprioc acid (EACA). Interferents were Hemolysis and Hemodilution levels above 40%.

SUMMARY OF CLINICAL PERFORMANCE DATA

Testing was performed at three clinical sites for Reference Ranges and Method Comparison.

Reference Ranges

Reference Ranges for the CORA PlateletMapping Assays were estimated using the CLSI C28-A3c Guideline on three reference sample groups. Blood samples from up to 55 normal volunteer subjects were taken at each of the three sites, for a total of approximately 150 samples (see below). Subjects were chosen representing demographic populations of the three areas, regarding age, race and gender. These reference ranges are shown below.

Assay	Heparinized Blood Parameter	N	Range
HKH	MA (mm)	149	53 - 68
ActF	MA (mm)	152	2 - 19
ADP	MA (mm)	145	45 - 69
AA	MA (mm)	144	51 - 71
ADP	% Aggregation	145	Abnormal < 83%
ADP	% Inhibition	145	Normal ≥ 83%
AA	% Aggregation	144	Abnormal < 89%
AA	% Inhibition	144	Normal ≥ 89%

Method Comparison

Method Comparison studies were conducted at three clinical sites on patient samples following CLSI EP09-A3 Guideline. The subjects enrolled were patients undergoing heart surgery or PCI procedures, with blood samples drawn pre- and post-surgery and in the ICU. Summary statistics are presented below.

Surgical Patients and Normal Donors (for CORA)								
All Sites	**ADP**				**AA**			
	Sensitivity		**Specificity**		**Sensitivity**		**Specificity**	
CORA	74.5%		82.9%		84.0%		86.5%	
(95% CI)	64.7%	to 82.8%	77.7%	to 87.4%	77.8%	to 89.0%	80.4%	to 91.2%
TEG 5000	94.9%		39.0%		88.4%		50.0%	
(95% CI)	88.5%	to 98.3%	29.7%	to 49.1%	82.8%	to 92.7%	29.1%	to 70.9%

CONCLUSIONS DRAWN FROM NON-CLINICAL AND CLINICAL TESTING

The data and information provided in this submission support a substantial equivalence determination for the CORA System with PlateletMapping Assay and the TEG 5000 Thromboelastograph Platelet Mapping Assay predicate device. Therefore, clearance of this 510(k) premarket notification for the CORA analyzer, with PlateletMapping Assay should be granted.